UNITED STATES PATENT AND TRADEMARK OFFICE

018512-00130US ASP

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/519,076	03/06/2000	Lawrence Salkoff	8512-00130US	8507

20350 7590 03/11/2003

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	12

DATE MAILED: 03/11/2003

Response Due 6/11/03 53P

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/519,076	Applicant(s) Salkoff et al
	Examiner Nirmal S. Basi	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 10, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-16, 22-44, 47, 49-52, and 54-56* is/are pending in the application.

4a) Of the above, claim(s) *1-16 and 22-44* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *47, 49-52, and 54-56* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The request filed on 2/10/03 (paper number 13) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/519076 is acceptable and a CPA has been established. An action on the CPA follows.

2. Amendment filed 2/10/03 (paper number 14) has been entered. Applicant has amended claims 47, 50, 52 and 55. Claims 47, 50-52, 54-56 will be examined as they pertain to the elected Group III, i.e. directed to isolated polypeptide comprising amino acid sequence of SEQ ID NO:16, being encoded by the nucleic acid of SEQ ID NO:17. Claims 47, 49, 52 and 54 contain non elected inventions (SEQ ID NOs:1, 3, and 18). The objection to claims 47, 49, 52 and 54 containing non elected inventions was presented in paper number 11 and is maintained. Applicant has not addressed examiners objection, nor amended the claims to remove reference to non-elected invention. Applicant must amend the claims to remove reference to non-elected invention.

Response to Applicants Arguments

Applicants arguments as pertaining to the claim rejections under 35 USC § 101 and 35 USC § 112, 1st paragraph are addressed below. Applicant argues the potassium channel of the present invention is expressed in spermatocytes. Applicants arguments have been fully considered and found persuasive. Claims 47, 50, 51, 52, 54-56 remain rejected, for reasons of record in paper number 7, under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The rejection is recast below to better

address the issues of utility under 35 USC § 101, especially in light of the reference of Schreiber et al, Exhibit A (J. Biol. Chem. Vol. 273, Issue 6, pages 3509-3516, February 6, 1998).

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 47, 50, 51, 52, 54-56 remain rejected, for reasons of record in paper number 7, under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Applicant and Dr. Timothy Jegla argued in paper number 10 (6/14/02) that intracellular pH has a profound effect on the viability of mammalian sperm, alkaline pH is necessary for sperm capacitation and acrosome reaction, sperm capacitation is accompanied by increase in potassium permeability that hyperpolarizes the membrane, and conclude since Slo3 is highly expressed in sperm and is activated by alkalization the Slo3 channel plays an important role in sperm capacitation and is an excellent target for candidate compounds that modulate sperm function. Applicants and Schreiber disclose claimed pH sensitive potassium

channel isolated from testis and is found in spermatocytes. Schreiber discloses although claimed potassium channel is found in testis the data does not exclude very low levels of expression or spatially restricted patterns of expression within the other tissues examined. The declaration of Dr. Timothy Jegla did not specifically state that claimed potassium channel protein is required for sperm capacitation and acrosome reaction. The argument is made that the claimed potassium channel protein has a profound effect on the viability of mammalian sperm and may be involved in sperm capacitation and acrosome reaction. Schreiber states, "Because of the its high testis-specific expression, pharmacological agents that target human Slo3 channels may be useful in both the study of fertilization as well as in the control or enhancement of fertility", also stated, "Because of its sensitivity to both pH and voltage, Slo3 could be involved in sperm capacitation and/or acrosome reaction, essential steps in fertilization where changes in both intracellular pH and membrane potential are known to occur". The specification nor prior at disclose that the claimed potassium channel functions predominantly in the spermatocytes or mature sperm, or that all potassium channels are involved in sperm capacitation and acrosome reaction. Schreiber postulates that a "missing factor" could be required that permits functionality in spermatocytes as compared to sperm. Schreiber also postulates, "However if mSlo3 expression is indeed largely restricted to spermatocytes, it may be that pairing of sensitivity to pH and voltage is designed to fulfil a unique role in spermatocytes. All proteins utilized by mature sperm are synthesized during spermatogenesis, as mature sperm lack transnational activity. Thus although the mSlo3 protein has not been identified in mature sperm, robust transcription in developing spermatocytes makes it likely that the channel

is present at these later stages. The unlikely alternative is that mSlo3 is utilized only during a narrow window of time in sperm development". Schreiber further disclose alkalization and depolarization are components of the signaling pathway during both sperm capacitation and the acrosome reaction, two essential steps preceding fertilization of oocyte. As the sperm membrane depolarizes, voltage-gated calcium channels open, permitting the entry of calcium and thereby triggering the release of the acrosomal granule. Schreiber specifically states, "Although the role of Slo3 in these processes remains speculative at this time, it is plausible that this channel plays a role in coordinating these events by directly linking cellular pH and membrane voltage". It is concluded that it is not known if the claimed potassium channel is found in mature sperm, its role in sperm capacitation and the acrosome reaction is speculative. Therefore based on the specification and prior art further research must be done to assign a utility that would meet the requirements 35 U.S.C. 101. Although the claimed polypeptide may be involved in sperm capacitation and the acrosome reaction there is no showing in the specification or prior art to conclude such a statement. Since the role in sperm capacitation and the acrosome reaction is speculative further research must be conducted to assign a role in sperm capacitation and the acrosome reaction.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed invention of claims 47, 49-52, 54-56.

The claims are directed to isolated polypeptide encoded by a nucleic acid that specifically binds under specified stringent conditions to the complement of a nucleic acid encoding an amino acid sequence of SEQ:16.

It appears from the specification that the nucleic acid of SEQ ID NOs: 17 encode the pH sensitive potassium channel (SEQ ID NO:16), the monomer having a unit conductance of approximately 80-120 pS when the monomer is in a functional tetramaric form, capable of transporting potassium ions, having increased potassium ion transporting activity above an intracellular pH of 7.1.

The applicant has mentioned general functional activities which may be applicable to known pH sensitive potassium channel proteins but not disclosed the function associated with the specific proteins encoded by the claimed nucleic acids. The specification discloses potassium channels are found in a wide variety of animal cells and "channels regulating these currents open and allow the escape of potassium under certain conditions. Potassium channels are also disclosed to be "involved

in diverse functions such as regulating arteriolar smooth tone", tuning of hair cell frequency, and modulation of transmitter release at nerve terminals". Although the claimed polypeptides of instant application encode potassium channels the specific result of changing potassium flux is not known. The specification discloses the Slo3, pH sensitive potassium channels can be used in screening inhibitors and activators, in methods of identifying homologs, in cellular transfection, and gene therapy. In light of the specification the skilled artisan can speculate that the polypeptide encoded by disclosed polynuceotides, and nucleic acid that hybridize to the disclosed nucleic acids of SEQ ID NOS:17, belong to the pH sensitive potassium channel proteins. However, apart from the disclosure of SEQ ID NO:16 no other disclosure is provided within the instant specification on the functional features the claimed potassium channel protein, nor are any disease states disclosed that are directly related to its dysfunction.

The utilities asserted by Applicant are not specific or substantial. Since no specific function of the polypeptides of instant invention, or polynucleotides that encode them, are known, and the hypothesized function is based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose the claimed polypeptide, useful to identifying drugs that affect said proteins and modulate their activity. Similarly, neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using claimed polypeptides. Thus the corresponding asserted utilities are essentially methods of using the claimed polynucleotide to identify other nucleic acids that hybridize to said polynucleotide, or to

isolate disease states associated with polypeptide disfunction, and as targets for drug discovery. Therefore the asserted utilities are essentially methods of isolating, testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating, isolating or testing for compounds that interact with the claimed polynucleotide, or encoded polypeptide, which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed polypeptides, further experimentation is necessary to attribute a utility to the claimed polypeptides and polynucleotide. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Accordingly, the instant specification provides insufficient guidance on "how to use" the claimed polypeptide of instant invention.

Claim Rejection, 35 U.S.C. 112, first paragraph

4. Claims 47, 50, 51, 52, 54-56 also remain rejected, for reasons of record in paper number 7, under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by

either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant argues based on the arguments filed in paper number 14, 2/10/02, to overcome rejection under 35 USC 101, rejection under 35 USC 112 First paragraph is also overcome, due to showing of utility. Applicants arguments have been fully considered but not found persuasive. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the polypeptides of instant invention, further experimentation is necessary to attribute a utility to the claimed polypeptides.

Although the claimed polypeptide is a potassium channel it utility is unknown, see rejection under 35 USC 101, above. Further, pertaining to the variants encompassed by the claims, the specification does not disclose the special technical feature of the invention that is required for activity . Applicant has not disclosed how to use the variant channel proteins which may have unit conductance of 80-120 ps, some structural similarity to Slo3 of SEQ ID NO:16, but be functionally different. There is no showing that all the polypeptides encompassed by the claims would have the same utility. Applicant has not shown how to use the functionally different variants.

Due to the large quantity of experimentation necessary to identify and purify active proteins encompassed by claims reciting hybridization, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said polypeptides, the unpredictability of the effects of mutation on the structure and function of proteins

(since mutations of SEQ ID NO:16, are also encompassed by the claim), undue experimentation would be required of the skilled artisan to make or use the claimed invention.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
March 10, 2003